

REMARKS

I. Status of the Claims

Claims 1-3, 6-12, 15, 18-26 and 46 are pending in the application and stand rejected. Claims 9 and 10 are objected to as depending from a rejected claim, but are otherwise considered allowable. The remaining claims stand rejected, variously, under 35 U.S.C. §102 and §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Objection to Claims 18-26

The examiner objects to claims 18-26 on the basis of dependency from a canceled claim. An amendment has been provided change the dependency to claim 6, which is still pending. Reconsideration and withdrawal of the objection is therefore respectfully requested.

III. Rejections Under 35 U.S.C. §102

A. Rowlands

Claims 1, 6 and 46 stand rejected as anticipated by Rowlands (WO93/01296). Applicants traverse.

The examiner states that “Rowlands teaches a method of obtaining vectors ... which are capable of expressing a plurality of a candidate antibody on the cell surface” Applicants have reviewed the entire Rowlands application can nowhere find a disclosure of cell surface expression – indeed, the application is focused on *secreted* expression. Assuming the examiner cannot point to such as disclosure, the “capable of” language of the rejection is insufficient to compensate for this deficit – either the reference teaches this step of the claimed method, or it does not. “A claim is anticipated only if each and every element as set forth in the claim is

found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Applicants submit that the reference fails to provide such a teaching, and thus the rejection is improper.

Reconsideration and withdrawal of the rejection is therefore respectfully requested.

B. Wigler *et al.*

Claims 1, 6, 7, 11, 12 and 46 stand rejected as anticipated by Wigler *et al.* (U.S. Patent 5,780,225). Applicants traverse.

Indeed, while Wigler *et al.* briefly address cell surface expression at column 13, lines 5-14, they provide no enabling technology for so doing. The only discussion of an actual cell surface expression relates to bacteriophage infection of *E. coli*, which is outside the scope of the present claims.

However, purely in the interest of advancing the prosecution, the claims have been amended to recite expression in yeast host cells, which the examiner admits is not disclosed in Wigler *et al.* Reconsideration and withdrawal of the rejection is therefore respectfully requested.

IV. Rejections Under 35 U.S.C. §103

A. Rowlands, Wigler *et al.* and Yokoyama

Claims 2, 3 and 8 are rejected as obvious over Rowlands or Wigler *et al.* in view of Yokoyama (U.S. Patent 5,646,011). According to the examiner, though Rowlands and Wigler *et al.* fail to provide a teaching of yeast host cells, Yokoyama corrects this deficiency, thereby render the rejected claim obvious. Applicants traverse.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP §§2143-2143.03.

Turning to Rowlands in view of Yokoyama, as discussed above, Rowlands fails to provide a teaching of cell-surface expression. Yokoyama also fails to provide such a teaching, and as such, the rejection is improper on its face and should be withdrawn.

With respect to Wigler *et al.* and Yokoyama, applicants submit that the combination of these references is suspect given that they are directed to completely different technologies. Wigler *et al.* teaches the expression of antibody populations in cells for the purpose of selecting those having a desired or modified binding profile. In general, the technology is directed at prokaryotic expression, but discussion of expression in "animal cells" is provided. Also, a passing reference is made to eukaryotic host cells, including the possibility of cell surface expression:

Methods of identifying antigen-binding molecule-expressing cells expressing an antigen-binding molecule of selected specificity other than the nitrocellulose filter overlay technique described above can be used. An important characteristic of any method is that it be useful to screen large numbers of different antibodies. With the nitrocellulose filter overlay technique, for example, if 300 dishes are prepared and 10^4 independent transformed host cells per dish are screened, and if, on average, each cell produces ten different antibody molecules, then $300 \times 10^4 \times 3$, or about 10^7 different antibodies can be screened at once. However, ***if the antibody molecules can be displayed***

on the cell surface, still larger numbers of cells can be screened using affinity matrices to pre-enrich for antigen-binding cells. There are immortal B cell lines, such as BCL₁B₁, which will express IgM both on the cell surface and as a secreted form (Granowicz, E. S., et al., J. Immunol., 125:976 (1980)). *If such cells are infected by retroviral vectors containing the terminal C μ exons, the infected cells will likely produce both secreted and membrane bound forms of IgM* (Webb, C. F., et al., J. Immunol., 143:3934-3939 (1989)). Still other methods can be used to detect antibody production....

Columns 13-14, bridging paragraph (emphasis added). Thus, at best, the reference teaches the use of bacteria, and suggests the *possibility* that animal cells may be used, additional surface expression in the latter being even *more* prospective in nature.

The examiner turns to Yokoyama for a teaching yeast cells. This is problematic for at least two reasons. First, the subject matter of Yokoyama is *completely* distinct from that of Wigler *et al.*, which as discussed above provides a general method for producing and screening antibody libraries. Yokoyama, in contrast, merely deals with the expression of a single, non-antibody molecule – a tumor protein designated cDNA62 that confers cisplatin sensitivity. Thus, the examiner, without any basis, has selected a secondary reference having almost *no* connection to the primary reference. Even under the most lenient of “motivation” standards, this combination fails, as explained below.

Except in narrow situations, it is *not* sufficient for obviousness that an invention merely have been “obvious to try.” As recently discussed by the Supreme Court, an obvious to try rationale *may* support a conclusion that a claim would have been obvious where one skilled in the art is choosing from *a finite number of identified, predictable solutions, with a reasonable expectation of success*. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct, 1727, 1742, 82 USPQ2d 1385, 1397 (2007). However, where obvious to try means that one would have to “vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical

or no direction as to which of many possible choices is likely to be successful ...,” that would not satisfy §103. *In re O’Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Similarly, where obvious to try means the exploring of “a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it ...,” that too would be insufficient. *Id.*

Here, there is clearly no “finite number of identified, predictable solutions” from which the skilled artisan could choose. Yet, the examiner has done exactly that in formulating this rejection. Moreover, the Patent Office almost universally takes the position that the biotechnology firmly resides in the realm of “the unpredictable arts.” Thus, the specific admonitions of the *KSR* court, with regard to motivation, have gone unheeded here.

Second, the examiner is effectively arguing that any technology found in Yokoyama can simply be “plugged in” to Wigler *et al.* Indeed, the secondary reference provides a *plethora* of molecule techniques and reagents, but the examiner has sought to pick *only that aspect of Yokoyama that is said to complete the rejection*, thereby ignoring the balance of the teachings of the reference.¹ “A prior art reference must be considered in its entirety, *i.e.*, as a *whole*, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).” MPEP §2141.02 (emphasis in original). Yet, the examiner has again ignored relevant legal doctrine in formulating this rejection, which clearly is improper.

For all of the foregoing reasons, applicants respectfully submit that the rejection improperly combines the primary and secondary references, and further constitutes an improper

¹ Indeed, in 36 columns, Yokoyama mentions yeast cells but three times.
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picking and choosing from the art. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

B. Rowlands, Wigler *et al.* and Slamon

Claim 15 is rejected as obvious over Rowlands or Wigler *et al.*, cited as above, in view of Slamon (U.S. Patent 4,918,162). Applicants traverse.

The examiner has admitted that neither Rowlands or Wigler *et al.* disclose use of yeast host cells, and there similarly is no such disclosure in Slamon. Given the amendment of claims to recite yeast host cells, this rejection also is improper. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

IV. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notice to that effect is earnestly solicited. Should the examiner have any questions, comments, or suggestions relating to this case, the examiner is invited to contact the undersigned applicants' representative at (512) 536-3184.

Respectfully submitted,



Steven L. Highlander
Reg. No. 37,642
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
512.536.3184 (voice)
512.536.4598 (fax)

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